

CLAIMS

1. An isolated nucleic acid encoding a B7-2 fusion protein comprising a nucleotide sequence encoding a first peptide having a B7-2 activity and a nucleotide sequence encoding a second peptide corresponding to a moiety that alters the solubility, binding affinity or valency of the first peptide.

2. The isolated nucleic acid of claim 1 which is a DNA.

3. The isolated nucleic acid of claim 2, wherein the first peptide comprises an extracellular domain of a human B7-2 protein.

4. The isolated nucleic acid of claim 3, wherein the first peptide comprises amino acid residues 24-245 of the sequence shown in Figure 8 (SEQ ID NO:2).

5. The isolated nucleic acid of claim 3, wherein the first peptide comprises a variable region-like domain of human B7-2.

6. The isolated nucleic acid of claim 3, wherein the first peptide comprises a constant region-like domain of human B7-2.

7. The isolated nucleic acid of claim 2, wherein the second peptide comprises an immunoglobulin constant region.

8. The isolated nucleic acid of claim 7, wherein the immunoglobulin constant region is a C γ 1 domain, including the hinge, CH2 and CH3 region.

9. The isolated nucleic acid of claim 7, wherein the immunoglobulin constant region is modified to reduce constant region-mediated biological effector functions.

10. The isolated nucleic acid of claim 9, wherein the biological effector function is selected from the group consisting of complement activation, Fc receptor interaction, and complement activation and Fc receptor interaction.

11. The isolated nucleic acid of claim 10, wherein the immunoglobulin constant region is a C γ 4 domain, including the hinge, CH2 and CH3 region.

12. The isolated nucleic acid of claim 11, wherein at least one amino acid residue of the CH2 domain is modified by substitution, addition or deletion.

5 13. An isolated B7-2 fusion protein comprising a first peptide having a B7-2 activity and a second peptide corresponding to a moiety that alters the solubility, binding affinity or valency of the first peptide.

10 14. The isolated B7-2 fusion protein of claim 13, wherein the first peptide comprises an extracellular domain of human B7-2 protein.

15 15. The isolated B7-2 fusion protein of claim 14, wherein the first peptide comprises amino acid residues 24-245 of the sequence shown in Figure 8 (SEQ ID NO:2).

16 16. The isolated B7-2 fusion protein of claim 14, wherein the first peptide comprises a variable region-like domain of human B7-2.

20 17. The isolated B7-2 fusion protein of claim 14, wherein the first peptide comprises a constant region-like domain of human B7-2.

25 18. The isolated B7-2 fusion protein of claim 13, wherein the second peptide comprises an immunoglobulin constant region.

30 19. The isolated B7-2 fusion protein of claim 18, wherein the immunoglobulin constant region is a Cy1 domain, including the hinge, CH2 and CH3 region.

35 20. The isolated B7-2 fusion protein of claim 18, wherein the immunoglobulin constant region is modified to reduce constant region-mediated biological effector functions.

21. The isolated B7-2 fusion protein of claim 20, wherein the biological effector function is selected from the group consisting of complement activation, Fc receptor interaction, and complement activation and Fc receptor interaction.

22. The isolated B7-2 fusion protein of claim 21, wherein the immunoglobulin constant region is a Cy4 domain, including the hinge, CH2 and CH3 region.

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23. The isolated B7-2 fusion protein of claim 22, wherein at least one amino acid residue of the CH2 domain is modified by substitution, addition or deletion.

5 24. A composition suitable for pharmaceutical administration comprising a fusion protein of claim 13 and a pharmaceutically acceptable carrier.

25. A composition suitable for pharmaceutical administration comprising a fusion protein of claim 14 and a pharmaceutically acceptable carrier.

10 26. A composition suitable for pharmaceutical administration comprising a fusion protein of claim 16 and a pharmaceutically acceptable carrier.

27. A composition suitable for pharmaceutical administration comprising a fusion protein of claim 18 and a pharmaceutically acceptable carrier.

15 28. A method for inhibiting an interaction of a B lymphocyte antigen, B7-2, with its natural ligand(s) on the surface of immune cells, comprising contacting an immune cell with a B7-2 fusion protein which inhibits B7-2 binding with its natural ligand(s), to thereby inhibit costimulation of the immune cell through the B7-2-ligand interaction.

20 29. The method of claim 28, wherein the B7-2 fusion protein comprises a first peptide having B7-2 activity and a second peptide comprising a moiety that alters the solubility, binding affinity or valency of the first peptide.

25 30. The method of claim 29, wherein the first peptide comprises an extracellular domain of the human B7-2 protein.

30 31. The method of claim 30, wherein the first peptide comprises amino acid residues 24-245 of the sequence shown in Figure 8 (SEQ ID NO:2).

32. The method of claim 29, wherein the second peptide comprises an immunoglobulin constant region.

35 33. The method of claim 32, wherein the immunoglobulin constant region is a Cγ1 domain, including the hinge, CH2 and CH3 region.

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34. A method for treating an autoimmune disease in a subject mediated by interaction of a B lymphocyte antigen, B7-2, with its natural ligand(s) on the surface of immune cells, comprising administering to the subject an inhibitory form of a B7-2 fusion protein, to thereby inhibit costimulation of the immune cells through the B7-2-ligand interaction.

35. The method of claim 34, wherein the inhibitory form of a B7-2 fusion protein is a B7-2 immunoglobulin fusion protein (B7-2Ig) comprising a first peptide comprising an extracellular domain of the B7-2 protein and a second peptide comprising an immunoglobulin constant domain.

36. The method of claim 35, wherein the extracellular domain of the B7-2 protein comprises amino acid residues 24-245 of the sequence shown in Figure 8 (SEQ ID NO:2).

37. A method for treating allergy in a subject mediated by interaction of a B lymphocyte antigen, B7-2, with its natural ligand(s) on the surface of immune cells, comprising administering to the subject an inhibitory form of a B7-2 fusion protein, to thereby inhibit costimulation of the immune cells through the B7-2 -ligand interaction.

38. An isolated variable region form of the B cell activation antigen B7-2 which comprises a B7-2 immunoglobulin-like variable region domain but does not comprise a B7-2 immunoglobulin-like constant region domain.

39. The B7-2 variable region form of claim 38, which is human.

40. The B7-2 variable region form of claim 38, which is a fusion protein comprising a B7-2 variable region polypeptide operatively linked to a heterologous polypeptide.

41. The B7-2 variable region form of claim 40, wherein the B7-2 variable region polypeptide is a human B7-2 variable region polypeptide.

42. The B7-2 variable region form of claim 41, wherein the human B7-2 variable region polypeptide comprises an amino acid sequence of about positions 24 to 133 of SEQ ID NO: 2.

43. The B7-2 variable region form of claim 40, wherein the heterologous polypeptide comprises an immunoglobulin constant region.

44. The B7-2 variable region form of claim 43, wherein the immunoglobulin constant region comprises the hinge, CH2 and CH3 domains of IgG1.

45. The B7-2 variable region form of claim 38, comprising a B7-2 immunoglobulin-like variable region domain operatively linked to a transmembrane domain, the B7-2 variable region form being expressed on the surface of a cell.

46. The B7-2 variable region form of claim 45, further comprising a non-B7-2 linker polypeptide located between the B7-2 immunoglobulin-like variable region domain and the transmembrane domain.

47. The B7-2 variable region form of claim 45, further comprising a cytoplasmic domain.

48. The B7-2 variable region form of claim 38, comprising a B7-2 immunoglobulin-like variable region domain bound to a solid support.

49. The B7-2 variable region form of claim 48, wherein the solid support is a bead or plate.

50. The B7-2 variable region form of claim 48, further comprising a non-B7-2 linker polypeptide located between the B7-2 immunoglobulin-like variable region domain and the solid support.

51. An isolated B7-2 fusion protein comprising a human B7-2 immunoglobulin-like variable region domain operatively linked to a heterologous polypeptide, wherein the B7-2 fusion protein does not comprise a B7-2 immunoglobulin-like constant region domain.

52. The B7-2 fusion protein of claim 51, wherein the human B7-2 immunoglobulin-like variable region domain comprises an amino acid sequence from about position 24 to position 133 of SEQ ID NO: 2.

53. The B7-2 fusion protein of claim 51, wherein the heterologous polypeptide comprises an immunoglobulin constant region polypeptide.

54. An isolated nucleic acid molecule encoding a variable region form of a B7-2 fusion protein, the B7-2 fusion protein comprising a human B7-2 immunoglobulin-like variable region domain operatively linked to a heterologous polypeptide, wherein the B7-2 fusion protein does not comprise a B7-2 immunoglobulin-like constant region domain.

55. The nucleic acid of claim 54, wherein the heterologous polypeptide is an immunoglobulin constant region polypeptide.

56. A recombinant expression vector comprising the nucleic acid molecule of claim 54.

57. A host cell containing the recombinant expression vector of claim 56.

58. An isolated nucleic acid molecule encoding a variable region form of B7-2, the nucleic acid comprising a contiguous nucleotide sequence encoding a signal peptide, a human B7-2 immunoglobulin-like variable region domain, a transmembrane domain and a cytoplasmic domain.

59. The nucleic acid molecule of claim 58, wherein the human B7-2 immunoglobulin-like variable region domain comprises an amino acid sequence from about position 24 to position 133 of SEQ ID NO: 2.

60. The nucleic acid molecule of claim 58, further comprising a nucleotide sequence encoding a non-B7-2 linker polypeptide located between the nucleotide sequence encoding the B7-2 immunoglobulin-like variable region domain and the transmembrane domain.

61. A recombinant expression vector comprising the nucleic acid molecule of claim 58.

62. A host cell containing the recombinant expression vector of claim 61, wherein the variable region form of B7-2 is expressed on the surface of the cell.

63. A method for stimulating a response by an activated T cell, comprising contacting the activated T cell with a variable region form of the B cell activation antigen B7-2, the variable region form of B7-2 comprising a B7-2 immunoglobulin-like variable region domain but not comprising a B7-2 immunoglobulin-like constant region domain such that a response by the activated T cell is stimulated.

64. The method of claim 63, wherein a T_{helper}-Type 2 (TH₂) response is preferentially stimulated.

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